Capture-Recapture Analysis and Pneumococcal Meningitis Estimates in England

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To improve estimates of disease incidence and deaths from pneumococcal meningitis among adults in England, we performed a capture-recapture analysis for 1996 through1999. We compared data from Hospital Episode Statistics (HES) and the Public Health Laboratory Services (PHLS) for incidence estimates and from HES and the Office for National Statistics (ONS) for estimates of deaths. Estimated sensitivities for the examined systems were 46% (95% confidence interval [CI] 42% to 50%) for HES and 40% [95% CI 37% to 44%] for PHLS. Sensitivities for mortality rates were found to be similar, 48% [95% CI 41% to 55%] for HES and 49% [95% CI 42% to 56%] for ONS. Stratification analysis showed that the sensitivity in those >85 years of age was significantly lower than the sensitivity for other ages. The estimated case-fatality rate was 24% [95% CI 21% to 26%]. These estimates indicate that a cost-benefit analysis of adult pneumococcal vaccination programs is required.

Streptococcus pneumoniae is a leading cause of pneumonia, bacteremia, meningitis, and otitis media in children and adults. In the United Kingdom, respiratory infections account for an estimated 55% of all antimicrobial drug prescriptions (1). The emergence of pneumococci that are resistant to single or multiple antimicrobial drugs (2,3) and their association with outbreaks in child care centers and nursing homes underscore the need for new preventive strategies (4).

Pneumococcal meningitis represents a small but important component of the total illness and deaths from pneumococccal disease, resulting in a mortality rate of 25% and sequelae in excess of 50% of affected cases (5,6). Public health officials have emphasized the prevention of pneumococcal meningitis and invasive pneumococcal disease (IPD) (7–10). Compelling data support administration of pneumococcal conjugate vaccine to children (11) and considerable, although arguably less robust, evidence supports the view that the elderly should receive pneumococcal vaccination with a polysaccharide vaccine (12,13). If pneumococcal vaccination is introduced into the general adult population, however, accurate estimates of the extent and impact of invasive pneumococcal disease are needed.

Geographic differences in the distribution of IPD and the underreporting of infectious diseases are widely acknowledged (14). As an alternative to population-based surveys and active surveillance systems, which are resource intensive, methods such as capture-recapture analysis (15) have been used effectively for both chronic disease and infectious disease epidemiology (16,17).

We performed a capture-recapture analysis to provide better estimates of illness and deaths caused by invasive adult pneumococcal disease among adults in England. We have focused on meningitis, which is the most reliably identifiable manifestation of invasive pneumococcal disease in the available U.K. data sources (18).

Materials and Methods

Data Sources

Hospital Episode Statistics (HES) and Public Health Laboratory Services (PHLS)-reconciled laboratory reports (RLR) on pneumococcal disease incidence for England were compared, and HES and Office for National Statistics (ONS) reports of deaths in England were compared. Private hospitals and private laboratories rarely manage bacterial meningitis in England. Each of the three sources—RLR, HES, and ONS—covers the entire population of England, 39.4 million adults ages $\geq$16 years in 1999. HES data were available only for hospitals in England, preventing an analysis of a larger U.K. dataset.

HES includes medical information on all patients treated in or admitted to National Health Service (NHS) hospi-

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tals in England. Diagnoses are recorded using the 10th International Classification of Diseases (ICD X) coding system, based on the clinical diagnosis, which may be supported by laboratory diagnostic data. RLR comprise data from laboratory reports of invasive disease from PHLS and NHS microbiology laboratories to PHLS Communicable Disease Surveillance Centre, and the PHLS Respiratory and Systemic Infection Laboratory, which actively collects pneumococcal isolates from invasive disease cases since 1996, in England. ONS contains reports of all certified deaths in England and Wales. Information on the cause of death is recorded by using the ICD IX coding system on the basis of the diagnosis made by the coroner or medical officer in charge of patient.

Extraction of Data

All adults in England >16 years of age in whom pneumococcal meningitis was diagnosed were identified from the three data sources. Mortality data were available for 17% of the RLR cases and were therefore unreliable. RLR data for the year 2000 were not available at the time of the study, and the HES data were recorded as encompassing financial years 1996–1999, that is, from April of the respective year to March of the consecutive year. Therefore, the incidence analysis was restricted to April 1996 to December 1999. The analysis of mortality rates was conducted by using records from April 1996 to March 2000. For case-fatality estimates, mortality rate data were restricted to December 1999 to be comparable with incidence data.

Cases were extracted from the RLR data when *S. pneumoniae* was isolated from cerebrospinal fluid (CSF) or when the clinical diagnosis recorded was pneumococcal meningitis; from HES when ICD X: G001 was recorded in the primary diagnostic field; and from the ONS data for England when pneumococcal meningitis (ICD IX: 3021) was the primary cause of death.

Identification of Duplicates

Two or more HES records were considered to be multiple records if the patient had the same date of birth and sex, if the reports were within 3 months of each other, and if the cases were reported from the same hospital NHS trusts. However, records with different hospital NHS trusts, but with the same date of birth, same sex, and within 3 months of each other were considered duplicates when a referral pattern between NHS trusts (i.e., in the same or adjacent regions) could be identified. The earliest record was retained from each duplicate set for analysis. RLR records were considered to be duplicates if they had same date of birth and sex, same laboratory, and had been collected within 3 months of each other, whereas for ONS records, date of death and place of death were also included as criteria.

Matching and Capture-Recapture Analysis

For the incidence data, HES and RLR records between April 1996 and December 1999 were matched if the person shared the same date of birth and sex and if the date of hospital admission was within ± 30 days of the specimen date. For the mortality estimates, HES and ONS records were matched on date of birth and sex, health authority (same or adjacent), and date of death within ±2 days of date of end of episode. The number of unreported cases and the total number of cases in the population, estimated according to Hook and Regal (19), can be estimated by the following formula:

$$\hat{x} = \left(\frac{ac}{b}\right); \ \hat{N} = a + b + c + \hat{x}$$

where *a* is the number of cases reported to source Z only; *b,* the-number of matched cases; and *c*, the number of cases reported to source Y only; $\hat{x}$, number of unreported cases by any source and is the estimated total number of cases in a population. Incidence and mortality rate were calculated by using mid-year population estimates for each corresponding year (ONS: population Estimates Unit). The analysis was stratified by age and year to check for consistency of estimates. A sensitivity analysis was carried out by using more or less stringent matching criteria for identification of duplicates, matching on region and age. The case-fatality rate was calculated from the estimated total number of deaths and the estimated total number of cases in the population. For each source, the sensitivity of the reporting systems was calculated as the number of cases of pneumococcal meningitis reported by either source divided by the number of cases estimated from the capture-recapture analysis.

Statistical Analysis

A bootstrapping method was used to calculate approximate 95% confidence intervals (CI) for the estimated unreported cases, the estimated total number of cases, and the estimated sensitivities of the two data sources. To test-for-trend in the sensitivities across groups, weighted least squares regression was used. Sensitivities were weighted by the estimated total number in the population. Analyses were performed with Stata software (Stata Corporation, College Station, TX).

Validation of Data Sources

To validate the diagnosis and matching in the data extracts, consultant microbiologists in all PHLS laboratories in the South West Region of England were sent line-listings of RLR and HES extracts relating to their laboratory and acute NHS trust (a public agency that provides secondary healthcare services to the population of a certain geographic area in the United Kingdom), respectively.

They then verified the correctness of diagnosis and matching, according to their own laboratory records. They also obtained details from their local NHS trust of hospital episode diagnoses of pneumococcal meningitis for cross-checking against RLR and HES records.

Results

Incidence

Between April 1996 and December 1999, a total of 668 isolates of *S. pneumoniae* from patients with meningitis were documented in RLR, and 1,069 cases of pneumococcal meningitis were recorded in HES. After multiple records (20 from RLR and 332 from HES) and 2 records from the RLR in which date of birth and age were missing were excluded, 646 records in RLR and 737 in HES were retained for analysis. The mean age in RLR (55.8 years [range 16–97]) and HES datasets (55.3 years [range 16–96]) was similar, as was the sex distribution (52% in both were male) (Table 1).

Matching was possible in only 296 cases, demonstrating an overlap of fewer than half the records between the datasets, and we estimated that an additional 521 (95% CI: 477 to 568) cases were not captured by either source. The capture-recapture analysis thus showed 1,608 (95% CI 1,483 to 1,747) cases of adult pneumococcal meningitis. The estimated sensitivities of the data collection systems were 40% (95% CI 37 to 44) for RLR and 46% (95% CI: 42 to 50) for HES (Table 2). Sensitivity estimates varied by year of reporting, but no evidence of a trend was shown across the years (Table 2) or the age-groups (Table 3). The lowest sensitivities were observed in those $\geq$85 (16% and 19% for RLR and HES, respectively) and the sensitivities of both data sources were significantly lower in this age group than in those $\leq$84 ($p = 0.002$ and $p = 0.03$ for RLR and HES, respectively; Table 3). The annual incidence rate determined by capture-recapture estimates decreased from 1.36 per 100,000 per annum in 1996–1997 to 0.78 per 100,000 per annum in 1998–1999.

Matched cases did not vary significantly from cases not recaptured, when examined by patient's age or gender or by year. The mean difference between the specimen date (RLR) and date of episode (HES) for the matched cases was 0.14 days (range 10–24), with 70% of cases having the same date recorded in both datasets. Information on other covariates was largely consistent within the matched records (Table 1).

Mortality Rates

Between April 1996 and March 2000, 197 deaths from pneumococcal meningitis in England were reported by ONS, whereas 195 deaths were recorded in HES. The mean age in ONS (61.7 years [range 16–96]) and HES datasets (62.7 years [range 16–97]) was similar and had the same sex distribution (50% were male).

Table 1. Summary of data on pneumococcal meningitis for ages $\geq$16 years in England from the data sources used, Reconciled Laboratory Reports (RLR), Hospital Episode Statistics (HES), and the matched cases

	RLR (%)	HES (%)	Matched (%)
Year			
1996/97	133 (20.6)	239 (32.4)	51 (17.2)
1997/98	182 (28.1)	194 (26.3)	80 (27.0)
1998/99	151 (23.4)	190 (25.8)	80 (27.0)
1999[a]	180 (27.9)	114 (15.5)	85 (27.7)
Total	646	737	296
Age group			
16–19	16 (2.5)	20 (2.7)	8 (2.7)
20–24	16 (2.5)	16 (2.2)	7 (2.4)
25–44	145 (22.3)	175 (23.7)	64 (21.6)
65–74	135 (21)	140 (19)	57 (19.3)
75–84	75 (11.6)	78 (10.6)	30 (10.1)
85+	21 (0.15)	24 (3.2)	4 (1.3)
Total	646	737	296
Region			
North and York	85 (11.5)	62 (9.6)	25 (8.45)
Trent	77 (10.5)	77 (12)	44 (14.86)
West Midland	72 (9.7)	54 (8.3)	18 (6.08)
North West	101 (13.7)	69 (10.7)	41 (13.85)
Eastern	84 (11.4)	64 (10)	42 (14.19)
London	117 (15.9)	183 (28.3)	44 (14.86)
South East	113 (15.3)	47 (7.3)	43 (14.53)
South West	88 (11.9)	90 (13.9)	39 (13.18)
Total	646	737	296
Sex			
F	301 (46.6)	353 (48.0)	137 (46.3)
M	336 (52)	382 (51.8)	159 (53.7)
NR	9 (1.4)	2 (0.2)	0 (0)
Total	646	737	296
Death status			
N	42 (6.5)	597 (81)	16 (5.4)
Y	64 (10)	140 (19)	19 (6.4)
NR	540 (83.6)	0 (0)	261 (88.2)
Total	646	737	296

[a]Data not available for January–March 2000.
[b]F, female; M, male; NR, not recorded; N, no death; Y, yes, death occurred.

Capture-recapture analysis indicated 107 (95% CI 75 to 150) adult deaths from pneumococcal meningitis not reported by either source, resulting in an estimated 404 (95% CI: 350 to 466) deaths. The estimated sensitivity of ONS and HES was 49% (95% CI 42% to 56%) and 48% (95%CI 41% to 55%), respectively. The number of deaths ascertained by HES increased significantly compared to those ascertained by ONS (test-for-trend $p = 0.03$ and $p = 0.51$, respectively). Mortality rate, similarly to incidence, decreased over the study years from 0.30 to 0.15 per 100,000 per annum; thus, the case-fatality rate did not change and was estimated at 24% (95% CI 21% to 26%) (Table 4).

Sensitivity Analysis of the Incidence Data

Application of less stringent criteria, that is, matching on age instead of date of birth, yielded an additional 13

Table 2. Capture-recapture analysis for the number of cases of pneumococcal meningitis among adults (≥16 years) in England, April 1996–December 1999, by period[a]

	No. records in data sources			Capture-recapture analysis			
Period	RLR[a]	HES[b]	Matched records	Unreported cases (95% CI)	Total no. cases in population (95% CI)	Sensitivity RLR% (95% CI) p = 0.30	Sensitivity HES% (95% CI) p = 0.67
Apr 1996–Mar 1997	195	239	82	216 (156 to 300)	568 (487 to 668)	34 (28 to 40)	42 (35, 49)
Apr 1997–Mar 1998	168	194	70	174 (121 to 248)	466 (393 to 556)	36 (29 to 43)	42 (34, 49)
Apr 1998–Mar 1999	172	190	99	67 (46 to 96)	330 (286 to 379)	52 (45 to 59)	58 (50, 65)
Apr 1999–Dec 1999[b]	111	114	45	101 (64 to 158)	281 (228 to 350)	39 (31 to 49)	40 (31, 50)
All study period April 1996–Dec 1999	646	737	296	521 (434 to 625)	1,608 (1,483 to 1,747)	40 (37 to 44)	46 (42, 50)

[a]RLR, reconciled laboratory reports; HES, Hospital Episode Statistics; CI, confidence interval.
[b]RLR data not available for January through March 2000.

matched records. This gave an estimate for the total number of cases in the population of 1,541 cases, yielding a sensitivity of 42% for HES and 48% for RLR. Application of more stringent matching criteria, including matching on region, increased the estimated number of cases from 1,608 to 2,061, giving a sensitivity of 31% and 36% for HES and RLR, respectively.

Validation of Data Sources by Using Regional Data

Data were validated in 13 of the 17 laboratories, which included 76 (88%) of the 86 RLR records and 75 (86%) of the 87 HES records identified as originating in the South West Region of England. Thirty-eight cases matched between the sources, yielding an estimated capture-recapture total of 150.

Of the 38 original matches, 37 were confirmed as correct from laboratory records. Two additional matches were identified (one incorrect date of birth in HES, one in RLR). Of the remaining 35 records in HES but not in RLR, 17 had no laboratory record, 9 had laboratory evidence of pneumococcal meningitis, 8 had positive blood cultures for *S. pneumoniae*, and 1 had been incorrectly reported (meningitis due to group B streptococci). Of the 36 records in RLR but not in HES, 33 documented positive CSF cultures for *S. pneumoniae*, 1 noted septic arthritis, and 2 had no laboratory record. An additional five cases were identified (three only in laboratory records and two only in hospital trust records) that were not in the main study. When the two additional matches, the two incorrect diagnoses, and the five additional cases were taken into account, the capture-recapture estimate was unchanged at 150 cases.

Discussion

This capture-recapture analysis provides evidence of underascertainment of both incidence of and deaths from adult pneumococcal meningitis in England by the national laboratory and clinically based reporting systems. All surveillance systems compared in the study captured less than half of the estimated cases or deaths in the population. The sensitivity of these systems to capture cases occurring in those >85 years of age was significantly lower than in the younger population. Our findings are similar to capture-recapture estimates of bacterial meningitis in Italy (20), and our estimates of case-fatality rate (24%) are similar to those reported elsewhere (16%-31%) (21).

Apart from incomplete reporting in the surveillance systems, underascertainment may arise from the absence of a specific diagnosis in the severely ill, particularly the elderly (22); the absence of a confirmed microbiologic diagnosis (23) or misclassification of known pneumococcal meningitis as unspecified or unknown meningitis due to failure to collect blood or CSF samples. An active surveillance study conducted in the United States concluded that deaths due to invasive pneumococcal disease may be

Table 3. Capture-recapture analysis for the number of cases of pneumococcal meningitis among adults (≥16 years) in England, April 1996 to December 1999, by age group

	No. records in the data sources			Capture-recapture analysis		Sensitivity	
Age (y)	RLR	HES	Matched records	Unreported cases (95% CI)[a]	Total no. cases in population (95% CI)	RLR % (95% CI)	HES % (95% CI)
16–24	32	35	15	23 (9 to 52)	75 (52 to 110)	43 (26 to 60)	47 (29 to 65)
25–44	145	175	64	140 (96 to 205)	396 (333 to 476)	37 (29 to 44)	44 (36 to 52)
45–64	238	284	126	140 (103 to 188)	536 (474 to 607)	44 (39 to 50)	53 (47 to 59)
65–74	135	140	57	114 (75 to 170)	332 (276 to 402)	41 (33 to 49)	42 (34 to 51)
75–84	75	78	30	72 (41 to 125)	195 (151 to 257)	38 (28 to 49)	40 (29 to 51)
85+[b]	21	25	4	89 (–)	131 (–)	16 (–)	19 (–)

[a]CI, confidence intervals.
[b]Due to small numbers in the matching records cell, it was not possible to calculate the CIs for this age group.

Table 4. Capture-recapture analysis for the number of deaths from pneumococcal meningitis among adults (≥16 years) in England, April 1996 to March 2000, by period

	No. of records in the data sources[a]			Capture-recapture analysis				
Period	ONS	HES	Matched records	Unreported deaths (95% CI)	Total no. of deathsin population(95% CI)	Sensitivity ONS % (95% CI)	Sensitivity HES % (95% CI)	Case-fatality %[b] (95% CI)
Apr 1996–Mar 1997	65	55	28	36 (18 to 66)	128 (98 to 167)	51 (38 to 64)	43 (31 to 55)	23 (19 to 27)
Apr 1997–Mar 1998	51	57	20	57 (30 to 113)	145 (106 to 208)	35 (23 to 48)	40 (26 to 53)	31 (26 to 37)
Apr 1998–Mar 1999	44	45	25	15 (7 to 31)	79 (59 to 104)	56 (41 to 70)	57 (42 to 71)	24 (19 to 31)
Apr 1999–Mar 2000	37	38	22	11 (4 to 24)	64 (46 to 85)	58 (42 to 74)	58 (43 to 75)	12 (9 to 18)
All study period April 1996–March 2000	197	195	95	107 (75 to 150)	404 (350 to 466)	49 (42 to 56)	48 (41 to 55)	24 (21 to 26)[c]

[a]ONS, Office of National Statistics; HES, Hospital Episode Statistics; CI, confidence interval.
[b]Based on the number of cases in Table 1.
[c]Excluding deaths from January 2000 to March 2000 to be comparable with the number of cases in Table 1.

underestimated by 15%-45% and suggested that these missed cases could potentially be reported as unspecified deaths (24).

Our main estimates for incidence and deaths were largely supported by the sensitivity analysis. The slightly lower sensitivities estimated for 1999 HES data may be explained by the incomplete data for that year (see Methods). One possible explanation for the decreasing incidence during the study period may be a decrease in the number of diagnostic lumbar punctures performed (25,26). For pneumococcal bacteremia, PHLS reports show a small increase in incidence following the implementation of the enhanced surveillance for IPD in 1996, which (with the exception of a 1997 peak) remained relatively constant (27,28).

Strengths and Limitations of the Study

The use of capture-recapture analysis to estimate the incidence and mortality rates from pneumococcal disease has some drawbacks (29). However, in the absence of large population–based surveillance, this method can provide good estimates of disease incidence and associated deaths (30). The English national data sources used were assumed to be the most representative and complete for pneumococcal meningitis. The data were collected in each of the data sources in parallel and in a nonselective manner. The assumption that sources are independent is rarely fully met in epidemiology (31). We assume some positive dependence, in that the laboratory confirmation of a case (RLR) is likely to lead to a notification to HES and, if death occurs, notification to ONS. This dependence would have, if anything, led to an underestimation of both incidence and mortality rates (32). Negative dependence is unlikely. A third source of data for pneumococcal meningitis in England (clinician notification data) was available but did not have sufficient personal identifiers to include in the analysis. Therefore, we were unable to quantify dependency between the sources used in analysis. The capture-recapture estimates of the annual number of cases decreased during the study period. However, the sensitivities are relatively constant over time and no evidence was found for a trend over time; thus, we believe that estimates of sensitivity for the whole study period are valid.

We assume that the probability of cases being captured to all sources was not influenced by the characteristics of the case. The cases derived from the datasets were similar in terms of age, gender and outcome. Recaptured cases did not vary significantly from cases not recaptured, when examined by age, sex, or year (Table 1).

Accuracy of Diagnosis and Matching

Some diagnostic misclassification of pneumococcal meningitis may have occurred during the recording of HES and the ONS data (33,34). However, as discussed previously, that misclassification of pneumococcal meningitis as meningitis cause unspecified or cause unknown was more likely to have occurred. Nevertheless, even if misclassification occurs, capture-recapture analysis normally provides more reliable estimates than routine surveillance systems (35).

The study's matching strategy was supported by results of the validation study conducted in the South West. This study showed that matching without names for these data sources had a high degree of accuracy. An acceptable level of accuracy of recording laboratory-confirmed cases was also found for both RLR and HES datasets, with only two false-positive diagnoses being identified. The capture-recapture estimate did not change after validation.

Meningitis represents <10% of adult invasive pneumococcal disease (36). If all invasive pneumococcal positive isolates from the RLR had been included, the probability of including false cases in RLR would have greatly increased, thus increasing the probability of false matches and leading to an overestimation of the total number of cases. The inclusion of nonspecified meningitis (ICD 10 = G00.9) would have led to a similar increase in the probability of including false-positive cases in HES, and similarly of overestimating the results.

We restricted the analysis to records of pneumococcal meningitis from the primary diagnosis field of HES records to avoid diagnoses not related to the reason for hospitalization and ensure precision of the estimates. As meningitis is commonly a serious condition, it is normally recorded as primary diagnosis in the first diagnostic field. An additional analysis including all diagnostic fields in HES gave only a marginal change in the sensitivities of the reporting systems (data not shown). Searching other diagnostic fields in the validation analysis did not identify any additional cases.

Possible Implications on Vaccine Prevention

Our capture-recapture analysis should be generalizable to other industrialized countries, with a similar epidemiology of adult pneumococcal meningitis and similar surveillance systems. Pneumococcal meningitis is associated with a high mortality rate and represents a reasonably robust indicator of the illness from invasive pneumococcal infection in the population (37). Therefore, this analysis should inform decision makers when considering prevention and control policies and orienting further research, as previous policies have been mainly based on PHLS data.

Studies suggest that rather than targeting high-risk groups, current vaccination policies for adults with pneumococcal polysaccharide vaccine (PPV) are most cost-effective if implemented for all persons >65 years (38; A. Melegaro, J. Edmunds, unpub. data). In the context of our revised estimates, the benefits of vaccination are likely to be even greater. Evaluation of the pneumococcal conjugate vaccination (PCV) indicates that population-based programs for infants and children are cost-effective compared with PPV or no vaccination (39,40). Mangtani et al. suggest that the conjugate vaccine may be more promising for preventing IPD among adults than PPV (41). Data from England and Wales show that the 7-valent PCV has about 77% of serotype coverage in adults >65 years of age and 51% in younger adults (27). Do our revised estimates of the incidence of and mortality rates from pneumococcal disease among adults justify PCV vaccination? We propose that a cost-benefit analysis of PCV vaccination of adults across a range of different ages is required. This analysis should take into account our revised estimates for incidence and deaths, the potential for immunologic boosting by further vaccination in old age, the impact of herd immunity, and the potential for a decrease in the carriage of antimicrobial-resistant strains (7,8,39–41).

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References

1. Frischer M, Heatlie H, Norwood J, Bashford J, Millson D, Chapman S. Trends in antibiotic prescribing and associated indications in primary care from 1993 to 1997. J Public Health Med 2001;23:69–73.
2. Cartwright K. Pneumococcal disease in western Europe: burden of disease, antibiotic resistance and management. Eur J Pediatr 2002;161:188–95.
3. Johnson AP, Speller DC, George RC, Warner M, Domingue G, Efstratiou A. Prevalence of antibiotic resistance and serotypes in pneumococci in England and Wales: results of observational surveys in 1990 and 1995. BMJ 1996;312:1454–6.
4. Nuorti JP, Butler JC, Crutcher JM, Guevara R, Welch D, Holder P, et al. An outbreak of multidrug-resistant pneumococcal pneumonia and bacteremia among unvaccinated nursing home residents. N Engl J Med 1998;338:1861–8.
5. Kornelisse RF, Westerbeek CM, Spoor AB, van der Heijde B, Spanjaard L, Neijens HJ, et al. Pneumococcal meningitis in children: prognostic indicators and outcome. Clin Infect Dis 1995;21:1390–7.
6. Kragsbjerg P, Kallman J, Olcen P, Pneumococcal meningitis in adults. Scand J Infect Dis 1994;26:659–66.
7. Moxon ER, Heath PT, Booy R, Azzopardi HJ, Slack MP, Ramsay ME. Conference on the impact of Hib conjugate vaccines in preventing invasive *H. influenzae* diseases in the UK. Vaccine 1999;17:S11–3.
8. ME, Andrews N, Kaczmarski EB, Miller E. Efficacy of meningococcal serogroup C conjugate vaccine in teenagers and toddlers in England. Lancet 2001;357:195–6.
9. Schuchat A, Robinson K, Wenger JD, Harrison LH, Farley M, Reingold AL, et al. Bacterial meningitis in the United States in 1995. Active Surveillance Team. N Engl J Med 1997;337:970–6.
10. Quick RE, Hoge CW, Hamilton DJ, Whitney CJ, Borges M, Kobayashi JM. Underutilization of pneumococcal vaccine in nursing home in Washington State: report of a serotype-specific outbreak and a survey. Am J Med 1993;94:149–52.
11. Black S, Shinefield H, Fireman B, Lewis E, Ray P, Hansen JR, et al. Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children. Northern California Kaiser Permanente Vaccine Study Center Group. Pediatr Infect Dis J 2000;19:187–95.
12. Sims RV, Steinmann WC, McConville JH, King LR, Zwick WC, Schwartz JS, The clinical effectiveness of pneumococcal vaccine in the elderly. Ann Intern Med 1988;108:653–7.
13. Fedson DS. Pneumococcal vaccination for older adults: the first 20 years. Drugs Aging 1999;15:21–30.
14. MacLehose L, McKee M, Weinberg J. Responding to the challenge of communicable disease in Europe. Science 2002;295:2047–50.
15. Capture-recapture and multiple-record systems estimation II: applications in human diseases. International Working Group for Disease Monitoring and Forecasting. Am J Epidemiol 1995;142:1059–68.
16. Abeni DD, Brancato G, Perucci CA. Capture-recapture to estimate the size of the population with human immunodeficiency virus type 1 infection. Epidemiology 1994;5:410–4.

17. Reintjes R, Termorshuizen F, van de Laar MJ. Assessing the sensitivity of STD surveillance in the Netherlands: an application of the capture–recapture method. Epidemiol Infect 1999;122:97–102.
18. Smith MD, Stuart J, Andrews NJ, Telfer Brunton WA, Cartwright KA. Invasive pneumococcal infection in South and West England. Epidemiol Infect 1998;120:117–23.
19. Hook EB, Regal RR. Capture-recapture estimation. Epidemiology 1995;6:569–70.
20. Faustini A, Fano V, Sangalli M, Ferro S, Celesti L, Contegiacomo P, et al. Estimating incidence of bacterial meningitis with capture-recapture method, Lazio Region, Italy. Eur J Epidemiol 2000;16:843–8.
21. Berg S, Trollfors B, Claesson BA, Alestig K, Gothefors L, Hugosso S, et al. Incidence and prognosis of meningitis due to *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Neisseria meningitidis* in Sweden. Scand J Infect Dis1996;28:247–52.
22. Le Moal G, Roblot F, Paccalin M, Pasdeloup T, Roblot P, Becq-Giraudon B. [Details of meningitis in the elderly]. Rev Med Interne 2000;21:844–53.
23. Newcombe J, Cartwright K, Palmer WH, McFadden J. PCR of peripheral blood for diagnosis of meningococcal disease. J Clin Microbiol 1996;34:1637–40.
24. Moore MR. Deaths due to invasive Streptococcus pneumoniae, United States 1996–1998(abstract 875). 39th Annual Meeting of the Infectious Disease Society of America (IDSA) , 25–28 October 2001, San Francisco, CA, 2001. Chicago: University of Chicago Press; 2001.
25. Ramsay M., Kaczmarski E, Rush M, Mallard R, Farrington P, White J. Changing patterns of case ascertainment and trends in meningococcal disease in England and Wales. Commun Dis Rep CDR Rev 1997;7:R49–54.
26. Jolly K, Stewart G. Epidemiology and diagnosis of meningitis: results of a five-year prospective, population-based study. Commun Dis Public Health, 2001;4:124–9.
27. George AC, Melegaro A. Invasive pneumococcal infection: England and Wales, 1999. CDR Wkly 2001;11.
28. Invasive pneumonococcal infection, England and Wales: 2000. CDR Wkly 2003;13:7–11.
29. Tilling K. Capture-recapture methods—useful or misleading? Int J Epidemiol 2001;30:12–4.
30. Hickman M, Cox S, Harvey J, Howes S, Farrell M, Frischer M, et al. Estimating the prevalence of problem drug use in inner London: a discussion of three capture-recapture studies. Addiction 1999;94:1653–62.
31. Hook EB, Regal RR. Capture-recapture methods in epidemiology: methods and limitations. Epidemiol Rev 1995;17:243–64.
32. Brenner H. Use and limitations of the capture-recapture method in disease monitoring with two dependent sources. Epidemiology 1995;6:42–8.
33. Williams JG, Mann RY. Hospital episode statistics: time for clinican to get involved? Clin Med 2002;2:34–7.
34. HES—The book. London: Department of Health;2000.
35. Brenner H. Effects of misdiagnoses on disease monitoring with capture-recapture methods. J Clin Epidemiol 1996;49:1303–7.
36. Laurichesse H, Romaszko JP, Nguyen LT, Souweine B, Poirier V, Guolon D, et al. Clinical characteristics and outcome of patients with invasive pneumococcal disease, Puy-de-Dome, France, 1994–1998. Eur J Clin Microbiol Infect Dis 2001;20:299–308.
37. Aszkenasy OM, George RC, Begg NT. Pneumococcal bacteraemia and meningitis in England and Wales 1982 to 1992. Commun Dis Rep CDR Rev 1995;5:R45–50.
38. Sisk JE, Moskowitz AJ, Whang W, Lin JD, Fedson DS, McBean AM, et al. Cost-effectiveness of vaccination against pneumococcal bacteremia among elderly people. JAMA 1997;278:1333–9.
39. Black S, Lieu TA, Ray GT, Capra A, Shinefield HR. Assessing costs and cost effectiveness of pneumococcal disease and vaccination within Kaiser Permanente. Vaccine 2000;19(Suppl 1):S83–6.
40. Lieu TA, Ray GT, Black SB, Butler JC, Klein JO, Breiman RF, et al. Projected cost-effectiveness of pneumococcal conjugate vaccination of healthy infants and young children. JAMA 2000;283:1460–8.
41. Mangtani P, Cutts F, Hall AJ. Efficacy of polysaccharide pneumococcal vaccine in adults in more developed countries: the state of the evidence. Lancet Infect Dis 2003;3:71–8.

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